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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FLOOD, MICHELE C	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 03/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/827,371	HUNG, DAVID	
	Examiner	Art Unit	
	Michele Flood	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 6-33* is/are pending in the application.

4a) Of the above claim(s) *12-21 and 28-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-11 and 22-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of the species, mannitol, in the reply filed on January 5, 2005 is acknowledged.

The originally elected species was not found; therefore the requirement for species election has been withdrawn. The Claims were examined on the merits taking each of the species of the Markush Group in Claims 1 into consideration.

Claims 1, 6-11 and 22-27 are under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6, 7, and 22-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for preparing for intraductal retrieval of fluid, cells and/or other material from a breast duct of a patient comprising administering intraductally to the patient an effective amount of mannitol that increases the ductal fluid collection from a breast duct of a patient, does not reasonably provide enablement for the claim-designated method comprising the intraductal administration of any and all amounts of any and all of the agents recited in the Markush group of Claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, as broadly claimed by Applicant.

The claims are drawn to a method for preparing for intraductal retrieval of fluid, cells and/or other material from a breast duct of a patient comprising administering intraductally to the patient an agent that increases the secretion of ductal fluid into a breast duct, wherein the agent is selected from the group consisting of hypotonic solution, a buffered solution, a nonabsorbable compatible solution, a protein, a colloid, a sugar, a protein, a colloid, a sugar, a polymer, mannitol, sorbitol, glucose, glycerol, sucrose, raffinose, fructose, lactulose, polyethyleneglycol (PEG), maltodextrin, dextran, dextran 70, hydroxyethyl starch, fluid gelatin, a synthetic colloid, an antibody, a binding protein, albumin, a hormone, a natural herb, an extract from a natural herb, silymarin, a surfactant, a growth factor, oxytocin, prolactin, an organic molecule, a muscle relaxant, and a ductal orifice dilator.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation added to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

While Applicant has reasonably demonstrated a method for preparing for intraductal retrieval of fluid, cells and/or other material from a breast duct of a patient comprising the intraductal administration of an effective amount of mannitol that

increases the ductal fluid into a breast duct, Applicant has not demonstrated a method comprising the intraductal administration of any and all of the agents recited in the Markush group of Claim 1 in any and all amounts to provide the claim-designated functional effect to increase secretion of ductal fluid into a breast duct of a patient. For instance, on page 14 of the specification, line 20 to page 16, Applicant exemplifies a method of intraductally administering an effective amount of mannitol in water to the breast of a rabbit to provide the claim-designated functional effect to increase ductal fluid collection. However, Applicant has not demonstrated a method for preparing for intraductal retrieval of fluid, cells and/or other material from a breast duct of a patient comprising the intraductal administration of any and any of the claim-designated agents in any and all amounts, wherein the intraductal administration of any of the claim-designated agents increase secretion of ductal fluid into the breast of a patient, as broadly claimed by Applicant.

While it may be possible that particular agents recited in the Markush group of Claim 1 could increase the secretion of ductal fluid into a breast duct of a patient such as hormones, it is highly unlikely that any and all of the claim-designated agents could increase secretion of ductal fluid into a breast duct. The Office notes that on page 5, lines 20-24, Applicant expressly states, "The invention is the discovery that by first artificially increasing the fluid volume or fluid reservoir in a breast one can collect sufficient ductal fluid for analysis of the duct and breast." On page 8 of the specification, lines 3-24, it appears that Applicant discloses that the intraductal administration of some of the claim-designated agents may not indeed increase secretion of ductal fluid but

rather increase or at least maintain the amount of collectable fluid already present in the lumen of the breast duct. It should be noted that the state of the art at the time the invention was made did not recognize that all of the instantly claimed agents could increase the secretion of ductal fluid into to the breast of a duct. For instance, Nikodem et al. (Birth, 1993, 20:61-64. *Do cabbage leaves prevent breast engorgement?*) teach that cabbage leaf extract discourages the secretion of fluid into the breast duct of a patient. There is no guidance in the specification, other than the administration of effective amounts of mannitol to increase ductal fluid collection from a breast duct. Moreover, the instant application does not provide a working example providing data which shows that the composition of the instant claims would indeed increase secretion of fluid into a breast duct of a patient comprising any of the claim-designated ingredients. Thus, Applicant has not demonstrated that any and all of the claim-designated agents have the claimed functional effect of increasing secretion of ductal fluid into a breast duct of a patient when intraductally administered to provide a method of preparing for intraductal retrieval of materials from a breast duct of a patient, as broadly claimed, other than the aforementioned and demonstrated disease condition.

Accordingly, it would take undue experimentation without a reasonable expectation of success for one skill in the art to make and/or use the method, as broadly claimed by Applicant.

Claims 1, 6, 7, and 22-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Applicant's claims are directed to a broad method for preparing for intraductal retrieval of fluid, cells and/or other material from a breast duct of a patient comprising administering to the patient an agent that increases secretion of ductal fluid into a breast duct, wherein the agent is selected from a recited Markush group comprising a plethora of numerous and agents representing very different constituents. It is acknowledged that Applicant has selected the species, mannitol, for prosecution on the merits. However, the written description is not commensurate in scope with the generic method claims encompassing a plethora of constituents having very different chemically and structurally different entities, which have not been adequately described nor evidenced to be in the possession of Applicant. Applicant broadly defines the agents that are useful in a method for preparing for intraductal retrieval of fluid, cells and/or other material from a breast duct, on page 4 of the present specification, line 25 to page 10, in its entirety. However, the specification as originally filed does not particularly point out or specifically distinguish agents that increase the secretion of fluid into a breast duct when the agent is intraductally administered thereto the breast duct of a patient. This rejection is made in part with particular regard to agents that are loosely defined by the following terms: a nonabsorable biocompatible solution, a protein, a colloid, a polymer,

a synthetic colloid, an antibody, a protein, an organic molecule, a ductal orifice dilator or a carbonated fluid comprising superoxygenated fluid that is colder than room temperature before administration, because this agents could constitute anything. Moreover, nowhere in the specification does Applicant provide written description that the agents increase secretion of materials into a breast duct of a patient when intraductally administered. "Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was 'ready for patenting' such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing or identifying distinguishing characteristics sufficient to show that the Applicant was in possession of the claimed invention", *see* Official Gazette, 1242 OG 172, January 30, 2001.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the at that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (*See* page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision.

The skilled artisan cannot envision from its enablement provision the detailed structure of the unidentified agents, *e.g.,* a nonabsorable biocompatible solution, a protein, a colloid, a polymer, a synthetic colloid, an antibody, a protein, an organic

molecule, a ductal orifice dilator or a carbonated fluid comprising superoxygenated fluid that is colder than room temperature before administration; and, thus conception is not achieved until reduction to practice has occurred. Adequate written description requires more than mere a statement that it is part of the invention and a reference to a potential method of isolating it. The product itself is required. Applicant has not described the aforementioned agents defined as having the functional effect to increase secretion of ductal fluid into a breast duct for use in the claim-designated method for preparing intraductal retrieval of materials from a breast duct of a patient with sufficient written description such that one skilled in the art would recognize that Applicant had possession of the claimed invention. *See Fiers v. Revel,* 25 USPQ 2d 1601 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Lts.,* 18 USPQ 2d 1016.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states

"An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention".

The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claim encompasses numerous species that are not further described. There is substantial variability among the species.

This is insufficient support to support the generic claims as provided by the Interim Written Description Guidelines published in June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Claim Objections

Claims 8-11 as amended remain objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 6, 22, 25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Falconer et al. (V), as evidenced by the teachings of Kartinos et al. (B) and Mullins (C).

On page 182, Column 2, lines 6-15, Falconer teaches a method for preparing for intraductal retrieval of fluid, cells and/or other material from a breast duct of a patient comprising administering intraductally to the patient prolactin (a growth hormone), ouabain or both dissolved in a solution of [Na+], [K+] and [Cl-] containing Dextran Blue 2000 (a nonabsorbable biocompatible solution, as evidenced by the teachings of Kartinos and Mullins). Falconer further teaches removing and sampling alveolar tissue

associated with the injected duct systems for water content determinations and Na+, K+ and Cl- and [14C]-lactose analysis, on page 184, Column 2, lines 29-33. In Table 1, Falconer shows that increasing the amounts of prolactin increased the water content of wet tissue in the treated mammary gland tissue. On page 184, Column 1, lines 13-19 bridging Column 2, lines 1-6, Falconer teaches *in vivo* intraductal injection of prolactin to a patient showed an increase [K+] of 10 mmol/kg wet tissue (see Table 3); whereas, *in vivo* intraductal administration of prolactin and ouabain an increase [Na+]. On page 182, Column 2, lines 14-19, Falconer teaches an increased extracellular water content of the ouabain-treated glands (*see* Table 3). Table 3 also shows an increased extracellular water content of the prolactin-treated glands, as well.

Falconer does not expressly teach his method for the intraductal administration of prolactin (a growth hormone), ouabain or both dissolved in a solution of [Na+], [K+] and [Cl-] containing Dextran Blue 2000 (a nonabsorbable biocompatible solution) to a patient as a method for preparing for intraductal retrieval of fluid, cells and/or other material from a breast of a patient comprising administering intraductally to the patient an agent that increases secretion of ductal fluid into a breast duct, wherein the agent is a nonabsorbable biocompatible solution. However, the method taught by Falconer is a one step process comprising the intraductal administration of the same ingredient, as disclosed by Applicant. Thus, a method for preparing for intraductal retrieval of fluid, cells and/or other material from a breast duct of a patient comprising administering intraductally to the patient an agent that increases secretion of ductal fluid into a breast

duct, wherein the agent is a nonabsorbable biocompatible solution, is inherent to the method of treatment taught by Falconer.

The reference anticipates the claimed subject matter.

Claims 1, 6, 22, 25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Martyn et al. (W), as evidenced by the teachings of Kartinos et al. (B) and Mullins (C).

Martyn teaches a method for preparing for intraductal retrieval of fluid, cells and/or other material from a breast duct of a patient comprising administering intraductally to the patient prolactin as either an emulsion or an aqueous solution, made by dissolving prolactin in NaOH and diluting with phosphate buffered saline containing Blue Dextran (a nonabsorbable biocompatible solution, as evidenced by the teachings of Kartinos and Mullins). The emulsion was prepared by sonicating an aqueous solution phase consisting of phosphate buffer saline containing bovine serum albumin and Blue Dextran with safflower oil (see page 323. Column 2, under *"Mammary intraductal injections"*. In Table 1, Martyn shows that glycerolipid synthesis in the mammary gland was significantly enhanced in the presence of insulin, corticosterone and prolactin; addition of prolactin stimulated acetyl-CoA carboxylase activity; prolactin together with insulin and corticosterone stimulated activity of fatty acid synthetase; glucose-6-phosphate dehydrogenase was enhanced with prolactin injection. On page 326, Column 1, lines 9-27, Martyn teaches that intraductal injection of prolactin, or prolactin

plus progesterone, had more secretion than did untreated emulsion treated or progesterone-treated glands within the same patient.

Martyn does not expressly teach his method for the intraductal administration of prolactin as either an emulsion or an aqueous solution, made by dissolving prolactin in NaOH and diluting with phosphate buffered saline containing Blue Dextran (a nonabsorbable biocompatible solution) to a patient as a method for preparing for intraductal retrieval of fluid, cells and/or other material from a breast of a patient comprising administering intraductally to the patient an agent that increases secretion of ductal fluid into a breast duct, wherein the agent is a nonabsorbable biocompatible solution. However, the method taught by Martyn is a one step process comprising the intraductal administration of the same ingredient, as disclosed by Applicant. Thus, a method for preparing for intraductal retrieval of fluid, cells and/or other material from a breast duct of a patient comprising administering intraductally to the patient an agent that increases secretion of ductal fluid into a breast duct, wherein the agent is a nonabsorbable biocompatible solution comprising an organic molecule, is inherent to the method of treatment taught by Martyn.

The reference anticipates the claimed subject matter.

Claims 1, 6 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Love et al. (*A).

Love the intraductal administration of physiological saline to a breast duct for the retrieval of fluid, cells and/or other material from a breast of a patient. In Column 6,

lines 55-67, Love discloses that "The volume of fluid introduced into the ductal network D_2 will be sufficiently large so that substantially the entire volume of the ductal network may be filled with the washing fluid and excess fluid will flow from the network as it is displaced by additional fluid input . . . The remaining fluid will continue to be introduced and will thus flush the cellular and other marker materials from the ductal network into the opening . . ." After collection of the washing fluid comprising the retrievable fluid obtained from the breast duct through a double lumen catheter, Love teaches analyzing the fluid to identify a marker of a breast condition (see Column 5, lines 38-44). Given the claims the broadest interpretation of the term "an organic molecule", the Examiner regards the physiological saline washing fluid taught by Love as an "organic molecule".

Love does not expressly teach, *per se*, her method for the intraductal administration of physiological saline as a method for preparing for intraductal retrieval of fluid, cells and/or other material from a breast of a patient comprising administering intraductally to the patient an agent that increases the secretion of ductal fluid from a breast duct, wherein the agent is an organic molecule. However, the method taught by Love is a one step process comprising the intraductal administration of the same ingredient, as disclosed by Applicant. Thus, a method for preparing for intraductal retrieval of fluid, cells and/or other material from a breast duct of a patient comprising administering intraductally to the patient an agent that increases secretion of ductal fluid into a breast duct, wherein the agent is a an organic molecule, is inherent to the method of treatment taught by Love.

The reference anticipates the claimed subject matter.

* Applicant is advised that the cited U.S. patents and patent application publications are available for download via the Office's PAIR. As an alternate source, all U.S. patents and patent application publications are available on the USPTO web site (www.uspto.gov), from the Office of Public Records and from commercial sources. Should you receive inquiries about the use of the Office's PAIR system, applicants may be referred to the Electronic Business Center (EBC) at http://www.uspto.gov/ebc/index.html or 1-866-217-9197.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele Flood whose telephone number is 571-272-0964. The examiner can normally be reached on 7:00 am - 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michele C. Flood

MICHELE FLOOD
PRIMARY EXAMINER

Michele Flood
Examiner
Art Unit 1654

MCF
March 21, 2005